UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,262	05/10/2006	Petra Peters-Wendisch	23369	5108

535 7590 07/23/2010

KF ROSS PC
5683 RIVERDALE AVENUE
SUITE 203 BOX 900
BRONX, NY 10471-0900

EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
07/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

EMAIL@KFRPC.COM
ereyes@kfrpc.com

Office Action Summary	Application No.	Applicant(s)	
	10/549,262	PETERS-WENDISCH ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/17/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8, 14-20, 26-28 were examined in the previous action. With supplemental amendment of this application, the applicant, on 11/17/08, cancelled claims 1-28 and added new claims 29- 39.

Applicants' arguments filed on 11/17/08 have been fully considered but they are found unpersuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objection

Claims 29-38 are objected to as being written in such poor English that the claims are barely understandable. Appropriate correction is required.

Claims 29-30 and 39 are objected in reciting "nucleotide sequence". Since nucleotide sequences are graphical representations of the order in which nucleotides are arranged in a nucleic acid, and sequences are not products, the claim should be amended to refer to a nucleic acid. Appropriate correction is required.

Claim 30 is objected to as being written in poor English. To enhance clarity and to be consistent with commonly used claim language, it is suggested the claim be amended to recite "the nucleic acid of claim 29, wherein nucleotides 506 to 918 of SEQ ID NO: 1 are completely deleted". Appropriate correction is required.

Claim 39 is objected in reciting "A probe for identifying and/or isolating a nucleotide sequence . . . of SEQ ID NO: 1, wherein the probe is….". It should be "a

probe for identifying and/or isolating the polynucleotide of SEQ ID NO: 1, wherein the probe is…." Appropriate correction is required.

Claim 39 is objected for following reason: It recites "--wherein the probe is a nucleotide sequence-. .". A probe is not a sequence. It should be amended to recite "wherein the probe is a nucleic acid selected from…: the nucleic acid of SEQ ID NO: 3; the nucleic acid of SEQ ID NO: 4; the nucleic acid of SEQ ID NO: 5; and the nucleic acid of SEQ ID NO: 6" . Appropriate correction is required.

Claim 31 is objected for reciting "A gene structure---- thereto". For clarity and consistency with commonly used claim language, the claims should be amended to recite, for example, "the nucleic acid of claim 29, wherein the nucleotide sequence of said nucleic acid is operably linked to a regulatory sequence". Appropriate correction is required.

Claim 32 is objected for reciting "A gene structure---- thereto". For clarity and consistency with commonly used claim language, the claims should be amended to recite, for example, "the nucleic acid of claim 30, wherein the nucleotide sequence of said nucleic acid is operably linked to a regulatory sequence". Appropriate correction is required.

Claims 33 is objected for reciting "A vector---- claim 31". It should read "a vector comprising the nucleic acid of 31". Appropriate correction is required.

Claims 34 is objected for reciting "A vector---- claim 32". It should read "a vector comprising the nucleic acid of 32". Appropriate correction is required.

Claim Rejection 35 U.S.C 112 2nd Paragraph

Claims 29-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29, 35 and 31-35, 37-38 (dependent on claim 29 or 36) are indefinite for the following reason: The term "a nucleotide sequence according to SEQ ID NO: 1, isolated from and replicable.....following microbial production of L-serine from a carbohydrate" is unclear and confusing. It is unclear how limitations regarding the level of expression in a microorganism of the family Corynebacteria are relevant to the claimed nucleic acid since the mutations required are in the coding region and expression is regulated upstream from the coding region. For examination purpose Examiner will interpret the claims as directed to an isolated nucleic acid comprising SEQ ID NO: 1 except that nucleotides 506 to 918 of SEQ ID NO: 1 have been completely deleted, partially deleted, or mutated, wherein said nucleic acid encodes an L-serine dehydratase having reduced enzymatic activity when compared to the enzymatic activity of the L-serine dehydratase of SEQ ID NO: 2 under the same conditions"

Claims 35-36 and 38 are indefinite for the following reason: the term "whose genome includes a series of endogenous .....to pyruvate following the microbial production of L-serine from a carbohydrate" is unclear and confusing for the following reasons. The term "further includes an endogenous nucleotide....homologously

recombined into the genome" makes no sense since on one hand the limitation appears to indicate that the nucleic acid is endogenous and in another it is stating that is recombinant by virtue of homologous recombination. Additional limitations such as the production of L-serine from a carbohydrate in a culture medium are redundant because it is understood that for L-serine to be produced, the cell has to be cultured in a medium that comprises a carbohydrate. The term "includes a series of endogenous SerA...Corynebacteria serine biosynthesis genes" is unclear because it appears as if Corynebacteria has more than one SerA-fbr, SerB and SerC gene. For examination purposes, it will be assumed that claim 35 reads "a recombinant microorganism belonging to the Corynebacteria family, wherein said microorganism comprises endogenous SerA-fbr, SerB and SerC genes, wherein said recombinant organism is obtained by introducing a modification within a gene encoding an L-serine dehydratase via homologous recombination, wherein said gene prior to being modified comprises SEQ ID NO:1, wherein the modification is made between nucleotides 506 and 918 of SEQ ID NO:1, wherein said modification is a mutation within nucleotides 506-918 of SEQ ID NO:1, the complete deletion of nucleotides 506-918 of SEQ ID NO:1, or a partial deletion within nucleotides 506-918 of SEQ ID NO:1, wherein the modified gene encodes an L-serine dehydratase having an enzymatic activity which is reduced compared to the enzymatic activity of the L-serine dehydratase of SEQ ID NO:2 under the same conditions". Claim 36 will be interpreted as being directed to the recombinant microorganism of claim 35 wherein the modified gene encodes a protein which no longer has L-serine dehydratase activity. It is unclear from claim 38 as to whether SEQ

ID NO:3 and SEQ ID NO:6 should be present in the modified gene. As such, the examiner will interpret claim 38 to be a duplicate of claim 36.

Claim Rejections 35 U.S.C 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed inventions 29-32 are rejected under 35 USC 101 because the claimed invention directed to non-statutory subject matter.

In the absence of the hand of man, naturally occurring genes are non-statutory subject matter (Diamond v. Chakrabarty, 206 USPQ 193 (1980). The genes of claims 29-32 are natural substances. The rejection may be overcome by amending claims 1 and 4 to recite wording such as an isolated or recombinant gene, or DNA.

Claim Rejections 35 U.S.C 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a variant of the polynucleotide of SEQ ID NO: 1 that has any mutation within the region corresponding to nucleotides 506-918 of SEQ ID NO: 1, wherein said variant encodes a protein having less L-serine dehydratase activity when compared to the L-serine dehydratase activity of the polypeptide of SEQ ID NO: 2, as well as any corynebacteria comprising said variant.

The specification only teaches an inactivating deletion within nucleotides 506-918 of the polynucleotide of SEQ ID NO:1. No additional mutations that would result in a variant encoding a protein having less L-serine dehydratase activity than the L-serine dehydratase activity of the polypeptide of SEQ ID NO: 2 have been disclosed. The specification fails to describe any other representative species by any identifying characteristics or properties other than having reduced/not having l-serine dehydratase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Argument

Applicants' arguments against rejection of the claims under 35 U.S.C. 112, first paragraph written description are acknowledged but not found persuasive. Applicants in their amendment argue that their polynucleotide is limited to polynucleotide having a deletion of position 506-918 of SEQ ID NO: 1 so that said polynucleotide encode a protein lacking serine dehydratase (sdaA) activity. Applicants' argument is considered but found unpersuasive. The claims require any type of mutations in the recited 506-918 region of SEQ ID NO: 1 that would result in an active enzyme, although not as active as the polypeptide of SEQ ID NO: 2. Specification does not provided other examples of mutations in the recited region that would provide a variant of the polypeptide of SEQ ID NO: 2 which is still enzymatically active but to a lesser degree with respect to the polypeptide of SEQ ID NO: 2.

Claims 29-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA molecule comprising all of SEQ ID NO: 1 except for nucleotides 506-918 of SEQ ID NO: 1, and a recombinant coryneform bacterium which has been modified to inactivate its endogenous gene encoding L-serine dehydratase, wherein said endogenous gene encoding L-serine dehydratase comprises SEQ ID NO: 1 prior to its inactivation, wherein said inactivation is due to the deletion of nucleotides 506-918 of SEQ ID NO: 1, does not reasonably provide enablement for a nucleic acid which is a variant of the polynucleotide of SEQ ID NO: 1 having any mutations in the region corresponding to nucleotides 506-918 of SEQ ID

NO: 1 that would encode an L-serine dehydratase having less enzymatic activity as compared to the L-serine dehydratase activity of the polypeptide of SEQ ID NO: 2 under the same conditions, or recombinant corynebacteria comprising said nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 29-34 are so broad as to encompass any nucleic acid which is a variant of the polynucleotide of SEQ ID NO: 1 having any number of unknown mutations in the region corresponding to nucleotides 506-918 of SEQ ID NO: 1, wherein said variant encodes an L-serine dehydratase having less enzymatic activity as compared to the L-serine dehydratase activity of the polypeptide of SEQ ID NO: 2 under the same conditions, and recombinant corynebacteria comprising said nucleic acid.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the lack of knowledge as to which mutations within nucleotides 506-918 of SEQ ID NO: 1 would result in an L-serine dehydratase with reduced enzymatic activity compared to the L-serine dehydratase activity of the polypeptide of SEQ ID NO: 2. variants of the polynucleotide of SEQ ID NO: 1 Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the

ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the deletion of a segment of the coding region which would result in an inactive enzyme.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable.

Argument

Applicants' arguments against rejection of the claims under 35 U.S.C. 112, first paragraph enablement requirement are acknowledged but not found persuasive as explained above. Applicants in their amendment argue that their polynucleotide is limited to polynucleotide having a deletion of position 506-918 of SEQ ID NO: 1 so that said polynucleotide encode a protein lacking serine dehydratase (sdaA) activity. Applicants' argument is considered but found unpersuasive because these claims are directed to a polynucleotide having any mutation in the recited 506-918 region of SEQ ID NO: 1 that would result in an active enzyme, although not as active as the polypeptide of SEQ ID NO: 1. To find out which mutations would result in reduced activity and which ones do not have an effect on activity would be required to conduct enormous amount of experimentation since the number of mutations that can be made in the region of nucleotides 506-918 of SEQ ID NO: 1 is extremely large and the

specification is silent with regard to which modifications are more likely to reduce enzymatic activity, with the exception of inactivating deletions. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

Claim Rejection - 35 U.S.C 102

The rejection of claims 35-36, 38 under 35 U.S.C. 102(b) as being anticipated by Kubota et al. (*Agr.Biol. Chem* 1985, vol. 49, pp 7-12,, from ids) is withdrawn after the amendment of claims make the rejection moot as the claims require deletion or mutations within residues 506-918 of SEQ ID NO: 1).

Claim Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made
>
> .

Claims 29-36 and 38 are rejected under 35 U.S.C. 103(a) by Kubota et al. (*Agr.Biol. Chem* 1985, vol. 49, pp 7-12, from ids) in view of Nakagawa et al. (US20020197605) . This rejection is necessitated by amendment

Kubota et al teach a coryneform bacteria having a mutated sdaA gene that encodes a protein having reduced sdaA activity and shows increased production of L-serine. However, Kobuta does not teach mutation in a serine dehydratase of SEQ ID NO: 1.

Nakagawa et al. teach a gene of SEQ ID NO: 1 of corynebacterium glutamicum which is 100% identical to applicants' serine dehydratase of SEQ ID NO: 1 isolated from corynebacterium glutamicum. Nakagawa et al. also teaches that said gene encodes a serine deaminase (another name for serine dehydratase). The gene of Nakagawa et al. comprises SEQ ID NO: 1 and encodes the same serine dehydratase that applicant teaches. L-serine is widely used in food and pharmaceutical industry. In L-serine producing bacteria (such as corynebacterium glutamicum) sdaA degrade L-serine (Kubota et al.).

One of skill in the art is **motivated, to** delete a significant portion or the entire gene of SEQ ID NO: 1 (sdaA of SEQ ID NO: 1 is taught by Nakagawa et al.) in *Corynebacterium glutamicum* for the benefit of completely inactivating the L-serine dehydratase so that said bacterium increases the production of L-serine. As such it would have been obvious to one of ordinary skill in the art to delete the whole gene or a

part of said gene so that the mutant *Corynebacterium glutamicum* will produce more L-serine.

Applicants argue that Kobuta et al teach a mutant *Corynebacterium glutamicum* where only a 32% reduction of sdaA activity is observed and that Kobuta et al perform undirected mutagenesis of sdaA gene of *Corynebacterium glutamicum*. This is not found persuasive. Kobuta et al do teach microorganism having a mutated sdaA gene that encodes a protein having reduced sdaA activity and shows increased production of L-serine. The 32% reduction is not an issue because the claims do not have any limitation as to how much reduction should be present. Deletion of the entire gene or a significant portion of the coding region would result in a completely inactive protein.

Applicants argue that though Nakagawa et al teach applicants' sdaA gene of SEQ ID NO: 1 from *Corynebacterium glutamicum,* Nakagawa did not delete serine dehydratase gene. Applicants argument is considered but not found persuasive. Nakagawa's gene of SEQ ID NO: 1 from *Corynebacterium glutamicum* is 100% identical to applicant gene of SEQ ID NO: 1 which is also isolated from *Corynebacterium glutamicum*. Nakagawa et al. also teaches that their gene of SEQ ID NO: 1 encodes a serine dehydratase. It is immaterial whether Nakagawa deleted their gene or not because the teachings of Nakagawa are not being introduced as teachings that show the deletion of said gene. They are simply included in the rejection to show that the nucleic acid of SEQ ID NO: 1 was known so that one of skill in the art could inactivate

it in *C. glutamicum* (a well known L-amino acid producer) for the benefit of increasing L-serine yields.

Conclusion

Claims 29-39 are rejected, and no claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah
Examiner, Art Unit 1652

/Delia M. Ramirez/
Primary Examiner, Art Unit 1652